

Ebola virus disease among male and female persons in West Africa

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later by cervical adenopathy, leukocytosis (17,700 white cells per cubic millimeter, with 5% anaplastic large-cell lymphoma cells), and respiratory distress due to interstitial lung involvement. Quantitative PCR testing performed on day 20 showed 117 copies of NPM-ALK per 10,000 copies of ABL and confirmed the relapse (Fig. 1B). Treatment with ceritinib (at a dose of 450 mg per square meter) was started on day 23 and induced a rapid clinical improvement, radiologic complete remission, and negative findings on quantitative PCR testing 113 days after discontinuation of crizotinib. Both patients remained in complete remission and continued to receive treatment.

In these two patients, residual neoplastic cells persisted for up to 3 years during crizotinib treatment. Quiescent stem cells have been shown to cause persistent PCR positivity and residual disease in chronic myeloid leukemia treated with imatinib, although they do not appear to interfere with the excellent prognosis of patients with the disease.⁵ These findings suggest that caution must be exercised when interrupting treatment in patients with ALK-positive lymphomas, since anaplastic large-cell lymphoma may recur rapidly. PCR testing to measure levels of NPM-ALK has limited ability to detect residual disease. The indicator of relapse may be the patient's clinical symptoms rather than the results of quantitative PCR testing or combined positron-emission tomography and CT.

Patients who have received crizotinib for early relapses after allogeneic bone marrow transplantation may be an exception. In these patients, temporary crizotinib treatment has resulted in durable remissions,² possibly because of an anti-ALK immune response mounted by the graft.

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Ebola Virus Disease among Male and Female Persons in West Africa

TO THE EDITOR: From December 2013 to August 11, 2015, a total of 20,035 confirmed and probable cases of Ebola virus disease (EVD) were reported in Guinea, Liberia, and Sierra Leone. There have been concerns that the different cultural roles or physiology of male and female persons may have resulted in the sexes being differently affected during this outbreak.^{1,2}

Data on confirmed, probable, and suspected EVD cases (according to World Health Organization [WHO] case definitions³) were collected with the use of a standard case-investigation form⁴ in Guinea, Liberia, Nigeria, and Sierra Leone. This form is completed when a case is detected and the patient is admitted to a health

care facility as part of the public health response to the outbreak. We used data on confirmed and probable EVD cases in Guinea, Liberia, and Sierra Leone to compare sex-specific epidemiologic patterns. Some records were not complete, but owing to the size and overall detail of the data, we assessed whether there were any differences according to sex.

Within each district, we compared the proportion of the population who were male with the proportion of patients with EVD who were male. For each country, we also tested for sex-related differences in incubation period, time from symptom onset to hospitalization, duration of hospitalization (separately for fatalities

Table 1. Analysis of Confirmed and Probable Cases of Ebola Virus Disease (EVD) in Guinea, Sierra Leone, and Liberia, According to Sex.*

Variable	Guinea			Sierra Leone			Liberia	
	Male Patients (N = 1763)	Female Patients (N = 1961)	P Value	Male Patients (N = 5436)	Female Patients (N = 5694)	P Value	Male Patients (N = 2602)	Female Patients (N = 2579)
Incubation period								
No. of patients	42	50		401	509		502	536
Mean days (95% CI)	9.7 (7.1–13.1)	11.2 (8.5–14.6)	0.26	10.6 (9.7–11.6)	10.9 (10.2–11.7)	0.32	9.9 (9.3–10.6)	10.4 (9.7–11.0)
Interval from symptom onset								
To hospitalization								
No. of patients	1187	1289		1515	1648		863	924
Mean days (95% CI)	5.1 (4.9–5.4)	4.6 (4.4–4.8)	<0.001	4.5 (4.3–4.7)	4.1 (3.9–4.3)	0.004	5.8 (5.5–6.2)	5.3 (5.0–5.7)
To death								
No. of patients	1154	1265		1244	1242		881	769
Mean days (95% CI)	7.8 (7.5–8.1)	7.3 (7.0–7.6)	0.01	6.7 (6.4–7.1)	6.5 (6.1–6.9)	0.17	9.2 (8.8–9.7)	8.9 (8.5–9.4)
To hospital discharge								
No. of patients	562	650		415	472		254	286
Mean days (95% CI)	17.0 (16.5–17.5)	17.0 (16.5–17.5)	0.49	14.8 (13.8–15.8)	14.7 (13.7–15.7)	0.46	17.3 (16.3–18.5)	17.2 (16.2–18.3)
Interval from hospitalization								
To death								
No. of patients	639	653		375	347		364	345
Mean days (95% CI)	4.3 (4.1–4.6)	4.4 (4.1–4.7)	0.36	4.6 (4.2–5.1)	5.1 (4.6–5.8)	0.09	4.2 (3.8–4.6)	4.6 (4.1–5.1)
To discharge								
No. of patients	524	616		202	247		209	224
Mean days (95% CI)	12.0 (11.6–12.5)	12.1 (11.7–12.6)	0.36	10.9 (9.9–12.1)	12.5 (11.3–13.8)	0.03	12.2 (11.2–13.4)	12.9 (11.8–14.1)
Case fatality rate†								
No. of patients	1415	1529		1426	1378		1796	1849
Rate (95% CI)	59.9 (57.3–62.5)	57.2 (54.7–59.7)	0.15	67.6 (65.1–70.0)	63.4 (60.8–66.0)	0.02	72.4 (70.3–74.5)	67.5 (65.3–69.6)
Reported exposure to a sick person — % (95% CI)‡	25.5 (23.4–27.6)	26.6 (24.7–28.6)	0.45	29.3 (28.1–30.6)	33.1 (31.9–34.4)	<0.001	37.2 (35.4–39.1)	42.7 (40.7–44.6)

* The number of patients is the number with available data for each variable. The means reported are from gamma distributions fitted to the observed data, and the sample sizes are the number of patients to which the gamma distributions were fitted. Observed mean intervals according to age group and sex are shown in Table S4 in the Supplementary Appendix.

† The case fatality rate is reported for patients with known final status and with a date of report before the date that the final status was entered into the database. The case fatality rate according to age group (in 5-year intervals) is reported in Table S8 in the Supplementary Appendix.

‡ The sample sizes for reported exposures are equal to the overall sample sizes reported for male and female patients in each country. Further details of reported exposures are provided in Table S15 in the Supplementary Appendix.

and survivors), case fatality rate, clinical signs and symptoms, and reported exposures to sick persons.^{4,5} We estimated the case fatality rate using recorded final status, excluding data from patients with a date of report on or after the date that the final status was entered into the database, as in our previous reports in the *Journal*.^{4,5}

Overall, 48.8% of the 20,035 confirmed and probable EVD cases were in male persons. The proportion of patients with EVD who were male (47.3% in Guinea, 50.2% in Liberia, and 48.8% in Sierra Leone) did not differ significantly from the proportion of the population who were male in any country (48.5% in Guinea, 50.0% in Liberia, and 48.2% in Sierra Leone) (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). However, the proportions were significantly different in Gueckedou district, Guinea, which had an unusually low proportion of patients who were male (36.6%, $P < 0.001$).

The average interval from symptom onset to hospitalization was approximately 0.5 days shorter among female patients than among male patients in all countries ($P < 0.05$ for all comparisons) (Table 1), driven by cases at the peak of the epidemic (Table S6 in the Supplementary Appendix). Female patients were significantly less likely to die than were male patients (case fatality rate, 63.0% vs. 67.1%; odds ratio, 0.83; 95% confidence interval, 0.77 to 0.91) (Table S8 and Section 3.3 in the Supplementary Appendix). This survival difference remained significant when we adjusted for age group (in 5-year intervals), clinical signs and symptoms, and interval from symptom onset to hospitalization (Section 3.4 in the Supplementary Appendix). In addition, although a higher proportion of female patients than male patients reported an exposure to a sick person, the number of exposures reported by female and male patients did not differ significantly (Section 3.5 in the Supplementary Appendix).

Results did not change significantly when we restricted the analysis to confirmed cases (80.8% of the 20,035 cases). Further details on all results are provided in the Supplementary Appendix.

We found that male and female persons have similar risks, on average, of EVD. However, there were significant differences — in particular, the higher survival rate among female patients. Male

patients spent 12.5% longer (approximately 12 hours) on average in the community while symptomatic, which could be particularly important if infectiousness increases after onset, making the risk of transmission in that last half-day higher than average. This suggests that, for control purposes, public health measures to reduce community-based transmission might benefit from awareness of sex-specific differences.

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